IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Heinz W. Gschwend et al.

Application No.: 10/566,856 Confirmation No.: 2175

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For: PYRIDAZINE DERIVATIVES AND THEIR USE AS THERAPEUTIC AGENTS Examiner: C. M. Jaisle

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DECLARATION BY VISHNUMURTHY KODUMURU UNDER 37 C.F.R. § 1.132

I, Vishnumurthy Kodumuru, hereby declare that:

1. I am a co-inventor of the subject matter described and claimed in the above-identified application, which relates to pyridazine derivatives and their use as therapeutic agents.

2. I or others prepared the compounds described in the specification and the compounds shown in the Table in the Appendix. These compounds can be prepared according to the Reactions Schemes described in the specification.

3. These compounds have been shown to be effective in inhibiting SCD1 either with high throughput screenings (HTS) according to procedures described in the specification or with enzyme inhibition assays (IC_{50}). The Table in the Appendix shows the data from the HTS and the IC_{50} values of these compounds.

4. All statements made of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

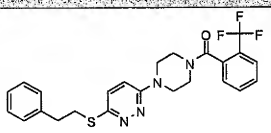
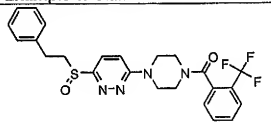
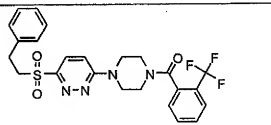
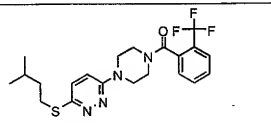
Respectfully Submitted,

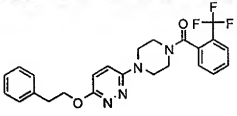
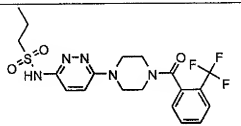
Date: March 17, 2008

Vishnumurthy Kodumuru

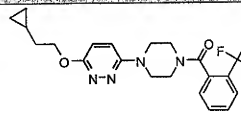
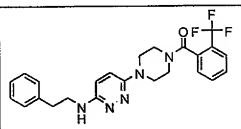
APPENDIX

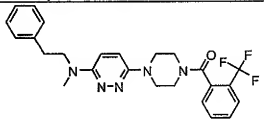
All of the compounds are active. Five of the compounds have IC_{50} data and were shown to be effective at inhibiting SCD1 activity *in vitro* at about 10 μM or less.

Chemical Name	Chemical Structure	Microsome IC_{50} (μM)	Cell IC_{50} (μM)
[4-(6-Phenethylsulfanyl-pyridazin-3-yl)-piperazin-1-yl]-(2-trifluoromethyl-phenyl)-methanone	 **Example 6/ Claim 22**	0.060	0.033
{4-[6-(2-Phenyl-ethanesulfinyl)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone	 **Example 4/ Claim 22**	0.067	0.175
{4-[6-(2-Phenyl-ethanesulfonyl)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone	 **Example 3/ Claim 22**	0.067	0.111
{4-[6-(3-Methyl-butylsulfanyl)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone	 **Example 6.1/ Claim 25**	0.447	0.849

Chemical Name	Chemical Structure	Microsome IC_{50} (μM)	Cell IC_{50} (μM)
[4-(6-Phenethyloxy-pyridazin-3-yl)-piperazin-1-yl]-(2-trifluoromethyl-phenyl)-methanone	 **Example 5/ Claim 14**	4.555	4.300
Propane-1-sulfonic acid {6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazin-3-yl}-amide	 **Example 2/ Claim 34**	6.250	10.527

Three of the compounds do not have IC_{50} data. However, based on their residual activity from the HTS, the predicted IC_{50}s still should qualify them as active compounds.

Chemical Name	Chemical Structure	Residual Activity (% Remaining, 1 μM)	Residual Activity (% Remaining, 10 μM)
{4-[6-(2-Cyclopropyl-ethoxy)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone	 **Example 5.1/ Claim 18**	53.875 Projected IC_{50} = 1-10 μM	29.330
[4-(6-Phenethylamino-pyridazin-3-yl)-piperazin-1-yl]-(2-trifluoromethyl-phenyl)-		91.144 Projected IC_{50} = 10-50 μM	55.946

Chemical Name	Chemical Structure	Residual Activity (% Remaining, 1 μM)	Residual Activity (% Remaining, 10 μM)
methanone	**Example 1.1/ Claim 29**		
{4-[6-(Methyl-phenethyl-amino)-pyridazin-3-yl]-piperazin-1-yl}-(2-trifluoromethyl-phenyl)-methanone	 **Example 1/ Claim 29**	86.210 Projected IC_{50} = 10-50 μM	57.955